

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
11 March 2004 (11.03.2004)

PCT

(10) International Publication Number
WO 2004/021010 A3

(51) International Patent Classification⁷: **G01N 33/574**,
C12Q 1/68, C07K 14/00, 16/30, C12N 15/11, A61K 38/00

ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO,
SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(21) International Application Number:
PCT/JP2003/010436

Declarations under Rule 4.17:

(22) International Filing Date: 19 August 2003 (19.08.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60-407,338 30 August 2002 (30.08.2002) US

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

(71) Applicants (for all designated States except US): ONCOTHERAPY SCIENCE, INC. [JP/JP]; 3-16-13, Shirokanedai, Minato-ku, Tokyo 108-0071 (JP). JAPAN AS REPRESENTED BY THE PRESIDENT OF THE UNIVERSITY OF TOKYO [JP/JP]; 3-1, Hongo 7-chome, Bunkyo-ku, Tokyo 113-8654 (JP).

— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

(72) Inventors; and

(75) Inventors/Applicants (for US only): NAKAMURA, Yusuke [JP/JP]; 17-33, Azamino 1-chome, Aoba-ku, Yokohama-shi, Kanagawa 225-0011 (JP). FURUKAWA, Yoichi [JP/JP]; 10-40, Miyazaki 3-chome, Miyamae-ku, Kawasaki-shi, Kanagawa 216-0033 (JP).

(74) Agents: SHIMIZU, Hatsushi et al.; Kantetsu Tsukuba Bldg. 6F, 1-1-1, Oroschi-machi, Tsuchiura-shi, Ibaraki 300-0847 (JP).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

Published:

— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
14 October 2004

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD OF DIAGNOSING COLON AND GASTRIC CANCERS

(57) Abstract: Objective methods for detecting and diagnosing Colorectal and gastric carcinomas are described herein. In one embodiment, the diagnostic method involves the determining a expression level of colon or gastric cancer -associated gene that discriminate between colon or gastric cancer and normal cell. The present invention further provides methods of screening for therapeutic agents useful in the treatment of colonic cancer and method of vaccinating a subject against colon or gastric cancer.

WO 2004/021010 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 03/10436

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/574 C12Q1/68 C07K14/00 C07K16/30 C12N15/11
A61K38/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C12Q C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, EMBASE, Sequence Search, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|--|
| X | <p>LIN Y.-M. ET AL.: "Molecular diagnosis of colorectal tumors by expression profiles of 50 genes expressed differentially in adenomas and carcinomas." ONCOGENE, vol. 21, 13 June 2002 (2002-06-13), pages 4120-4128, XP002270817 cited in the application the whole document</p> <p>----- -/--</p> | <p>1-8, 17-25, 27-31, 36-40, 47-49</p> |

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

19 February 2004

Date of mailing of the international search report

17.02.04

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Giry, M

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|---|
| X | KITAHARA O. ET AL.: "Alterations of gene expression during colorectal carcinogenesis revealed by cDNA microarrays after laser-capture microdissection of tumor tissues and normal epithelia." CANCER RES., vol. 61, 1 May 2001 (2001-05-01), pages 3544-3549, XP002270818 cited in the application the whole document | 1-8, 17-25, 27-31, 36-40, 47-49 |
| X | ZEMBUTSU H. ET AL.: "Genome-wide cDNA microarray screening to correlate gene expression profiles with sensitivity of 85 human cancer xenografts to anticancer drugs." CANCER RES., vol. 62, 15 January 2002 (2002-01-15), pages 518-527, XP002270819 the whole document | 1-8, 17-25, 27-31, 36-40, 47-49 |
| X | IIZAKA M. ET AL.: "Expression profile analysis of colon cancer cells in response to sulindac or aspirin." BIOCHEM. BIOPHYS. RES. COMM., vol. 292, 29 March 2002 (2002-03-29), pages 498-512, XP002270820 the whole document | 1-8, 17-25, 27-31, 36-40, 47-49 |
| X | US 2002/086296 A1 (MEYERS R.A.) 4 July 2002 (2002-07-04) paragraph '0007! - paragraph '0066! paragraph '0076! - paragraph '0078! paragraph '0090! - paragraph '0093! claims 1-36; figure 4; example 2 | 1-8, 17-25, 27-31, 36-40, 47-49 |
| Y | WO 02/18565 A (BAYER AG) 7 March 2002 (2002-03-07) the whole document | 1-8, 17-25, 27-31, 36-40, 47-49 |
| Y | WO 02/42777 A (AVENTIS PHARMA DEUTSCHLAND GMBH) 30 May 2002 (2002-05-30) the whole document | 1-8, 17-25, 27-31, 36-40, 47-49 |

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|---|
| P,A | WO 02/097074 A (BAYER AG) 5 December 2002 (2002-12-05) the whole document | 1-8, 17-25, 27-31, 36-40, 47-49 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP 03/10436

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 26, 39-40, 42-43
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 39-40 and 42-43, due to the step of "administering a pharmaceutically effective amount of ..." are directed to a method of treatment of the human/animal body by therapy, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 19, 44-46, 50
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-8, 17-25, 27-31, 36-40, 47-49 (all in part)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 39-40 and 42-43, due to the step of "administering a pharmaceutically effective amount of ..." are directed to a method of treatment of the human/animal body by therapy, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Claims Nos.: 26, 39-40, 42-43

Claim 26 : Rule 39.1(v) PCT - Presentation of information

Claims 39-40, 42-43 : Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box I.2

Claims Nos.: 19, 44-46, 50

Present claim 19 which relates to "a plurality of colon cancer-associated genes", concerns an extremely large number of possible methods. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the methods claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Therefore, the subject-matter of claim 19 has not been searched.

Present claims 44-45 which do not contain any technical feature to characterize a "method for inducing an anti tumor immunity" so lack clarity (Art. 6 PCT) and support in the description (Art. 5 PCT) that no meaningful search can be carried out (Art. 6 PCT).

Present claims 46 and 50 relate to a compound defined by reference to a desirable characteristic or property, namely "obtained/selected by the method according to any one of claims 27-35".

The claims cover all compounds having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for such products/compounds/methods/apparatus. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, no search has been carried out

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

for these claims because no such compounds are mentioned in the description.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

| Patent document cited in search report | | Publication date | Patent family member(s) | | Publication date |
|---|----|---------------------|----------------------------|---------------|---------------------|
| US 2002086296 | A1 | 04-07-2002 | US | 2003180930 A1 | 25-09-2003 |
| | | | AU | 4546301 A | 17-09-2001 |
| | | | WO | 0166765 A2 | 13-09-2001 |
| <hr/> | | | | | |
| WO 0218565 | A | 07-03-2002 | AU | 9378001 A | 13-03-2002 |
| | | | WO | 0218565 A2 | 07-03-2002 |
| <hr/> | | | | | |
| WO 0242777 | A | 30-05-2002 | DE | 10058596 A1 | 06-06-2002 |
| | | | AU | 2487502 A | 03-06-2002 |
| | | | WO | 0242777 A2 | 30-05-2002 |
| | | | EP | 1405079 A2 | 07-04-2004 |
| | | | US | 2002136717 A1 | 26-09-2002 |
| <hr/> | | | | | |
| WO 02097074 | A | 05-12-2002 | WO | 02097074 A2 | 05-12-2002 |